(b) determining whether the agent modulates at least one of the phenotypes.

REMARKS

I. Amendments

Claims 1-15 and 17-22 are canceled. New claims 24-33 are being added. The newly added claims do not add new matter and are completely supported by the application as originally filed. More particularly, support for claims 24-28 directed to transgenic mice having a disruption in a mTMT gene and exhibiting one or more of decreased body weight, decreased thymus weight, decreased thymus weight to body weight ratio and increased pre-pulse inhibition, methods of producing said transgenic mice and cells and tissues isolated from said mice may be found, for example, at page 11, lines 14-27, page 14, lines 25-30, page 15, lines 2-9, page 34, lines 20-24, page 24, lines 15-32 and page 53, lines 3-7 of the specification. Support for claim 34, directed to a transgenic mouse comprising a heterozygous disruption in a mTMT gene may be found, for example at page 15, lines 7-15 of the specification. Claims 29-31 directed to a targeting construct and methods of producing the targeting construct are supported, for example, at pages 9-11, at page 51, lines 15-32, and page 53, lines 3-7 of the specification. Support for claim 32 directed to transformed cells may be found, for example, at page 3, lines 4-14 of the specification. Lastly, support for claim 33 directed to methods of identifying agents that modulate a phenotype may be found, for example, at page 3-4, lines 3-7 of the specification.

Amendments to the claims are made without prejudice to the pending or now canceled claims or to any subject matter pursued in related applications. Moreover, the amendments are made solely to expedite prosecution of the application and are not intended to limit the scope of the invention. Applicants reserve the right to prosecute any canceled subject matter at a later time or in a later filed divisional, continuation or continuation-in-part application.

Upon entry of the amendments, claims 24-33 are pending in the instant application.

II. Rejections

A. Rejection under 35 U.S.C. § 112, first paragraph

Claims 5-15 and 17-22 were rejected under 35 U.S.C. § 112, first paragraph, as not

enabling one skilled in the art to make the invention commensurate with the scope of the claim. Applicants respectfully traverse this rejection. However, in view of the cancellation of Claims 5-15 and 17-22, the Examiner's rejection under 35 U.S.C. § 112, first paragraph, is moot.

Claims 1-5, 8, 9, and 11-15 were rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way to reasonably convey to one skilled in the relevant art that the Applicant, at the time the application was filed, had possession of the claimed invention. In particular, the Examiner asserts that the specification fails to teach transgenic animals and cells containing a disruption in "tryptase genes" other than mTMT and in other species of animals besides mice. Applicants respectfully traverse this rejection. However, in view of the cancellation of Claims 1-5, 8, 9 and 11-15, the Examiner's rejection under 35 U.S.C. § 112, first paragraph, is moot.

Applicants submit that new claims 24-33 are fully enabled by the teachings of the specification. As the rejection under 35 U.S.C. § 112, first paragraph of claims 1-15 and 17-22 is no longer relevant as a result of the cancellation of these claims, and new claims 24-33 are fully enabled by the teachings of the specification, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 112, first paragraph.

B. Rejection under 35 U.S.C. § 112, second paragraph

Claims 12 and 14 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Applicants respectfully traverse this rejection. However, as a result of the cancellation of claims 12 and 14, the Examiner's rejection is moot. Withdrawal of the rejection under 35 U.S.C. § 112, second paragraph, is respectfully requested.

Applicants submit that new claims 24-33 are definite and particularly point out and distinctly claim the subject matter regarded as the invention in accordance with 35 U.S.C. § 112, second paragraph.

C. Rejection under 35 U.S.C. § 103

Claims 1-15 and 17-22 were rejected as being unpatentable under 35 U.S.C. § 103(a) based upon the teachings of Wong *et al.*, 1999, *Journal of Biological Chemisty* 274(43):30784-30793 ("Wong") and Smyth *et al.*, 1996, *Journal of Leukocyte Biology* 60:555-562 ("Smyth") further in view of Capecchi *et al.*, 1989, *TIG* 5(3):70-76 ("Capecchi"). Applicants respectfully

traverse this rejection. However, as result of the cancellation of claims 1-15 and 17-22, the rejection is moot.

New claims 24-33 are non-obvious over the teachings of the prior art references. More particularly, the claimed invention relates to the *in vivo* mammalian characterization of the function of the mTMT gene, and provides transgenic animals and cells comprising disruptions in mTMT genes and methods and compositions relating thereto, which are not obvious in view of the teachings and disclosures of the references cited by the Examiner.

According to the Examiner, Wong teaches the identification and cloning of the murine (mTNMT) and the human (hTMT) transmembrane trypase genes. The Examiner acknowledges that Wong does not teach the use the mTMT gene to generate knockout mice or targeting constructs.

Smyth, according to the Examiner, teaches granzymes which are a family of serine proteases. The Examiner contends that Smyth advocates that the creation of knockout mice deficient in granzymes should elucidate their precise role and biological function. Further, the Examiner contends that Smyth thus teaches that knockout mice are a good model to study the function of tryptases and thereby proved the motivation to generate knockout mice having a disruption in a mTMT gene.

The disclosures of Wong and Smyth are absent of any teaching or suggestion of disrupting the mTMT gene, and in particular, to produce the transgenic mice, targeting constructs, tissues, cells, and methods as recited in the pending claims. In particular, the disclosures of Smyth or Wong, alone or in combination do not teach all of the limitations of the pending claims. Specifically, Wong and Smyth do not teach the targeting construct, methods of making the targeting construct, transgenic mice exhibiting one or more of decreased body weight; decreased thymus weight; decreased thymus weight to body weight ratio; and increased pre-pulse inhibition, methods of making the transgenic mice, cells and tissues derived from the transgenic mice, and methods of identifying agents that modify a phenotype, that are related to a disruption in the mTMT gene as claimed in the present invention.

As the obviousness rejection is no longer relevant as result of the cancellation of claims 1-15 and 17-22, and new claims 24-33 are not obvious in view of the teachings of Wong, Smyth and Capecchi, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 103.

It is believed that the claims are in condition for allowance, and notice to that effect is respectfully requested. The Commissioner is hereby authorized to charge any deficiency or credit any overpayment to Deposit Account No. 50-1271 under Order No. R-372.

Respectfully submitted,

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Enclosures